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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,433	05/10/2002	Bastian Nuyen	14620-012US1	4574

26161 7590 11/12/2009

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EXAMINER	
WINSTON, RANDALL O	
ART UNIT	PAPER NUMBER
1655	

NOTIFICATION DATE	DELIVERY MODE
11/12/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	09/622,433	NUYEN ET AL.	
	Examiner	Art Unit	
	Randall Winston	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-16,18,19,26-28,50 and 53-70* is/are pending in the application.

4a) Of the above claim(s) *9-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7,8,12-16,18,19,26-28,50 and 53-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0709*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement is made of the receipt and entry of the response to the amendment filed on 07/09/2009.

Claims 1-4, 7-8, 12-16, 18-19, 26-28, 50 and 53-62 and new claims 63-70 have been examined on the merits. (Claims 9-11 remains withdrawn from consideration)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 7-8, 12-16, 18-19, 26-28, 50 and 53-70 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Crumb et al. (US 6,030,943) in view Bobee et al. (5,438,072) for the reasons set forth in the previous OFFICE ACTION which are restated below.

Applicant claims a pharmaceutical composition and a kit comprising firstly of a vial of a lyophilized didemnin preparation comprised of a didemnin compound, a water-soluble material and an alkanol/water mixture wherein water is present for solubilization of the water soluble material and secondly of a vial of a reconstitution solution of mixed solvents and wherein the reconstitution solution of mixed solvents comprised a surfactant (i.e. nonionic), alkanol and water wherein alkanol (i.e. ethanol) is present for solubilization of the didemnin compound in the lyophilized didemnin preparation to be used for the injectable administrated to a subject and also whereas the lyophilized

dideminin preparation is also stable for at least 6 months and whereas the reconstituted pharmaceutical composition is also stable for at least 24 hours.

Crumb et al. teach a pharmaceutical composition may be in form of a container (i.e. a kit is a container and the container described in Crumb is a sterile ampoule) comprising firstly of a lyophilized didemnin preparation comprised of a didemnin (i.e. aplidine and dehydrodidemnn) and a water soluble material (i.e. mannitol) and water secondly a reconstitution solution comprised of a carrier such as water used for the purpose of aiding in the injectable administration of the pharmaceutical to a subject (see, e.g. column 5 lines 66-67 and column 6 lines 12-20).

Crumb, however, does not expressly teach that the claimed active ingredient of a surfactant and/or alkanol (i.e. ethanol) are mixed with water within Crumb's reconstitution solution wherein water is present for solubilization of the water soluble material as well as Crumb does not teach alkanol are mixed within a lyophilized didemnin preparation wherein alkanol (i.e. ethanol) is present for solubilization of the didemnin compound in the lyophilized didemnin preparation. Furthermore, Crumb does not expressly teach the claimed active ingredients' amounts/ranges.

Although Crumb does not expressly teach within his reference that surfactant and/or alkanol are mixed with water within Crumb's reconstitution solution, Crumb does teaches that one of ordinary skill in the art would want to utilize surfactant and/or wetting agents within its pharmaceutical formulation and/or container (see, e.g. column 6 lines 5-11). Therefore, it would have been obvious to one of ordinary skill in the art to just place the surfactant and/or wetting agents taught within Crumb's reference within

Crumb's taught reconstitution solution because surfactants and/or wetting agents are well known in the art to be effective carriers to aid in the injectable administration of an active ingredient such as didemnin compound to a subject.

Furthermore, Bobee benefically teaches that the claimed mixture of alkanol (i.e. ethanol), surfactants (i.e. Cremophor EL) and water are benefically used for the solubilization of a drug and/or compound in order for that drug and/or compound to become in the injectable form of administration of the claimed active drug and/or compound to a subject (see, e.g. entire document including abstract, tables and claims).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Crumb et al.'s pharmaceutical composition and/or kit to include the solubilization active ingredient mixture of an alkanol (i.e. ethanol), surfactant and water as taught by Bobee within Crumb's pharmaceutical composition and/or kit because the combined teachings as a whole would create the claimed pharmaceutical composition and/or kit for enhanced injectable delivery and/or administration of the pharmaceutical composition's active ingredient such as the claimed didemnin compound to a subject. Moreover, when the combined teachings as a whole combination of active ingredients as the claimed invention's combination of active ingredients are mixed in combination within the claimed concentrations with one another within a composition, the combined teachings combination of active ingredients as a whole would intrinsically produce and/or obtain the same claimed functional effects and/or intrinsic claimed properties (i.e. the same intrinsic claimed composition and/or intrinsic claimed active ingredients stabilizing properties). Furthermore, the adjustment

of other conventional working conditions (e.g. the substitution of one functional equivalent alkanol for another, determining suitable amount/ranges of each active ingredient within the claimed composition to create solubilization of the pharmaceutical composition, the substitution of one surfactant for the other and placing the reconstitution solution within a container such as a vial), is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

Accordingly, the claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Please note that the patentability of a product does not depend upon the method of production. If the product in a product by process claim is the same as or obvious from a product of the prior art, then the claim is unpatentable even though the prior art product was made by a different process. (see, e.g. MPEP 2113).

Please note, the intended use of the above claimed composition does not patentably distinguish the composition, per se, since such undisclosed use is intrinsic to the pharmaceutical composition reasonably suggested by the cited references, as a whole. In order to be limiting, the intended use must create a structural difference between the claimed composition and the prior art composition. In the instant case, the

intended use does not create a structural difference, thus the intended use is not limiting (see, e.g., MPEP 2112).

Applicant's arguments have been carefully considered but they are not deemed persuasive. Applicant argues a list of Crumb's contemplated "carriers, excipients, and diluents" that happens to include "mannitol" within the Crumb's composition. Secondly, Applicant argues there is nothing in Crumb's passage that would have led one to want to utilize surfactant and/or wetting agents and thus, the term surfactants does not even appear in this passage. Thirdly, Applicant argues a reconstitution solution is not even mentioned in Crumb, let alone a suggestion to use mixed solvent reconstitution solution comprising a non-ionic surfactant, an alkanol and water for injection. Fourthly, Applicant argues Bobee has nothing to do with reconstituting a lyophilized preparation, much less one that includes two substances that are quite dissimilar with respect to their solubility in water. Fifthly, Applicant argues that there is nothing in either Crumb or Bobee that would have led one to do so, much less expect this modification to result in lyophilized didemnin preparations having long term stability. Lastly, Applicant argues that there is nothing in Crumb and/or Bobee that would have led one to reasonably expect that combining the specific disclosure in the manner claimed would have resulted in kits and reconstituted pharmaceutical compositions.

Although Applicant argues a list of Crumb's contemplated "carriers, excipients, and diluents" that happens to include "mannitol" within Crumb's composition, Applicant

argument is not found persuasive it appears to Examiner that Crumb discloses in column 5 lines 66-67 and column 6 lines 1-11 that mannitol used as a suitable carrier, excipients and diluents for compounds and/or other active ingredients can be included within Crumb's pharmaceutical composition to be administered by injection.

Secondly, although Applicant argues there is nothing in Crumb's passage that would have led one to want to utilize surfactant and/or wetting agents and thus, the term surfactants does not even appear in this passage, Applicant argument is not found persuasive because it appears to Examiner that Crumb discloses in column 6 lines 5-11 that one of ordinary skill in the art would want to utilize surfactant and/or wetting agents within its pharmaceutical formulation and/or container. Therefore, Examiner maintains that it would have been obvious to one of ordinary skill in the art to just place the surfactant and/or wetting agents taught within Crumb's reference within Crumb's taught reconstitution solution because surfactants and/or wetting agents are well known in the art to be effective carriers to aid in the injectable administration of an active ingredient such as didemnin compound to a subject.

Thirdly, although Applicant argues a reconstitution solution is not even mentioned in Crumb, let alone a suggestion to use mixed solvent reconstitution solution comprising a non-ionic surfactant, an alkanol and water for injection, Applicant argument is not found persuasive because it appears to Examiner that Crumb discloses in column 6 lines 17-20 a reconstitution solution comprised of a carrier such as water used for the purpose of aiding in the injectable administration of the pharmaceutical to a subject. Moreover, although Crumb does not mention the use of a mixed solvent reconstitution

solution comprising a non-ionic surfactant, an alkanol and water for injection, Bobee remedies Crumb deficiency because Bobee benefically teaches that the claimed mixture of alkanol (i.e. ethanol), surfactants (i.e. Cremophor EL) and water are benefically used for the solubilization of a drug and/or compound in order for that drug and/or compound to become in the injectable form of administration of the claimed active drug and/or compound to a subject.

Fourthly, although Applicant argues Bobee has nothing to do with reconstituting a lyophilized preparation, much less one that includes two substances that are quite dissimilar with respect to their solubility in water, Applicant argument is not found persuasive because as stated above, although Crumb does not expressly teach that the claimed active ingredient of a surfactant and/or alkanol (i.e. ethanol) are mixed with water within Crumb's reconstitution solution, Bobee remedies Crumb deficiency because Bobee benefically teaches that the claimed mixture of alkanol (i.e. ethanol), surfactants (i.e. Cremophor EL) and water are benefically used for the solubilization of a drug and/or compound in order for that drug and/or compound to become in the injectable form of administration of the claimed active drug and/or compound to a subject.

Fifthly, although Applicant argues that there is nothing in either Crumb or Bobee that would have led one to do so, much less expect this modification to result in lyophilized didemnin preparations having long term stability, Applicant argument is not found persuasive because Examiner maintains that when the combined teachings as a whole (i.e. Crumb in view of Bobee) combination of active ingredients as the claimed

invention's combination of active ingredients are mixed in combination within the claimed concentration with one another within a composition, the combined teachings as a whole combination of active ingredients would intrinsically produce and/or obtain the same claimed functional effects and/or intrinsic claimed properties (i.e. the same intrinsic claimed composition and/or intrinsic claimed active ingredients stabilizing properties).

Lastly, although Applicant argues that there is nothing in Crumb and/or Bobee that would have led one to reasonably expect that combining the specific disclosure in the manner claimed would have resulted in kits and reconstituted pharmaceutical compositions, Applicant argument is not found persuasive because Examiner maintains that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Crumb et al.'s pharmaceutical composition and/or kit to include the solubilization active ingredient mixture of an alkanol (i.e. ethanol), surfactant and water as taught by Bobee within Crumb's pharmaceutical composition and/or kit because the combined teachings as a whole would create the claimed pharmaceutical composition and/or kit for enhanced injectable delivery and/or administration of the pharmaceutical composition's active ingredient such as the claimed didemnin compound to a subject.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Randall Winston whose telephone number is 571-272-0972. The examiner can normally be reached on 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

RW

/Christopher R. Tate/
Primary Examiner, Art Unit 1655